



Summary of Studies Supporting USDA Product Licensure

Establishment Name	Intervet Inc.
USDA Vet Biologics Establishment Number	165A
Product Code	1201.20
True Name	Bovine Virus Diarrhea Vaccine, Modified Live Virus
Tradename(s) / Distributor or Subsidiary (if different from manufacturer)	Bovilis Vista BVD CFP - Merck Animal Health
Date of Compilation Summary	June 26, 2019

Disclaimer: Do not use the following studies to compare one product to another. Slight differences in study design and execution can render the comparisons meaningless.

Study Type	Efficacy
Pertaining to	Bovine Viral Diarrhea Virus Type 1 (BVDV1)
Study Purpose	To demonstrate efficacy against respiratory disease caused by BVDV1.
Product Administration	
Study Animals	Bovine
Challenge Description	BVDV Type 1b NY-1 strain
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	February 20, 2004

Study Type	Efficacy
Pertaining to	Bovine Viral Diarrhea Virus Type 1 (BVDV1)
Study Purpose	To demonstrate efficacy against persistent infection of calves caused by BVDV1.
Product Administration	
Study Animals	Bovine
Challenge Description	BVDV Type 1b, strain SD02 BVD09
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	June 23, 2005

Study Type	Efficacy
Pertaining to	Bovine Viral Diarrhea Virus Type 1 (BVDV1)
Study Purpose	To demonstrate efficacy against fetal infection caused by BVDV1 206 days after vaccination.
Product Administration	
Study Animals	Bovine
Challenge Description	BVDV Type 1b strain SD02 BVD09
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	October 6, 2005

Study Type	Efficacy																																				
Pertaining to	Bovine Viral Diarrhea Virus Type 1 (BVDV1)																																				
Study Purpose	To demonstrate efficacy against respiratory disease caused by BVDV1 1 year after vaccination.																																				
Product Administration	1 dose administered by the subcutaneous route																																				
Study Animals	34 seronegative calves, 3 – 4 weeks of age; 22 vaccinates, 12 controls																																				
Challenge Description	All calves were challenged with BVDV1b strain T1186a at 1 year (365 days) after vaccination.																																				
Interval observed after challenge	All calves were monitored daily for 14 days post-challenge for clinical signs of disease. White Blood Cell (WBC) count and nasal shedding were determined daily for 10 days post-challenge.																																				
Results	<p><u>Leukopenia:</u> An affected calf was one that showed a > 40% decrease in white blood cell counts during the observation period.</p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># Affected</th> <th>Percent (%)</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>22</td> <td>2</td> <td>9</td> </tr> <tr> <td>Controls</td> <td>12</td> <td>12</td> <td>100</td> </tr> </tbody> </table> <p><u>Virus Shedding:</u> An affected calf was one in which nasal virus shedding was detected on any day post-challenge.</p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># Affected</th> <th>Percent (%)</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>22</td> <td>0</td> <td>0</td> </tr> <tr> <td>Controls</td> <td>12</td> <td>11</td> <td>92</td> </tr> </tbody> </table> <p><u>Clinical Observations:</u> An affected calf showed signs of acute BVDV1 (i.e. moderate to severe diarrhea, nasal discharge, and/or depression) during the observation period.</p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># Affected*</th> <th>Percent (%)</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>22</td> <td>1</td> <td>4.5</td> </tr> <tr> <td>Controls</td> <td>12</td> <td>6</td> <td>50</td> </tr> </tbody> </table> <p>Requirements per 9 CFR 113.311 were met.</p> <p>Raw data shown on attached pages.</p>	Group	# of Animals	# Affected	Percent (%)	Vaccinates	22	2	9	Controls	12	12	100	Group	# of Animals	# Affected	Percent (%)	Vaccinates	22	0	0	Controls	12	11	92	Group	# of Animals	# Affected*	Percent (%)	Vaccinates	22	1	4.5	Controls	12	6	50
Group	# of Animals	# Affected	Percent (%)																																		
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Controls	12	11	92																																		
Group	# of Animals	# Affected*	Percent (%)																																		
Vaccinates	22	1	4.5																																		
Controls	12	6	50																																		
USDA Approval Date	July 11, 2014																																				

White Blood Cell (WBC) Counts

Group	ID	WBC Counts (x 10 ³ /mL) Day Post-Challenge										
		-2	-1	0	2	3	4	5	6	7	8	10
Controls	308	16.7	13.2	10.5	11.1	5.1	4.9	6.1	5.5	8.2	8.2	9.3
	315	10.9	7.1	7.9	6.2	4.8	3.7	4.6	4.4	5.2	7.9	6.4
	319	11.6	9.5	8.7	9.5	5.2	5.4	6.5	6.5	6.5	8.9	7.0
	320	10.6	8.4	6.2	6.8	3.9	3.3	4.4	3.7	5.3	6.0	6.4
	322	12.5	11.0	9.1	11.5	5.3	3.7	5.9	5.6	7.6	11.6	7.8
	325	11.4	9.3	8.0	7.3	4.1	3.9	4.7	4.1	4.8	1.9	6.1
	327	14.7	12.7	9.8	11.6	7.1	5.3	8.3	6.7	7.9	9.2	9.7
	330	12.6	10.4	9.2	7.8	4.8	4.6	7.1	5.4	5.9	7.8	6.8
	334	10.0	10.1	9.4	10.7	6.7	5.6	6.8	5.9	7.0	9.5	7.7
	336	11.3	8.8	7.9	7.4	4.8	3.9	4.7	3.7	4.3	6.2	6.1
337	11.4	8.8	7.5	9.3	4.6	4.1	5.1	4.5	4.5	6.9	9.1	
338	13.7	11.3	10.4	10.2	6.2	5.6	5.0	5.2	5.6	7.7	8.8	
	Ave.:	12.3	10.1	8.7	9.1	5.2	4.5	5.8	5.1	6.1	7.7	7.6
Vaccinates	309	13.4	6.5	8.0	8.1	8.4	7.7	8.5	7.8	7.3	8.0	8.7
	310	13.6	10.7	9.6	9.9	8.9	8.7	11.0	9.8	11.1	8.0	9.9
	311	13.4	10.5	7.7	8.2	2.2	8.7	8.5	7.1	9.3	10.3	7.7
	312	12.5	11.3	8.7	9.1	9.1	8.0	6.5	7.3	9.2	8.0	10.3
	313	10.2	9.4	7.4	6.8	6.4	6.3	7.6	8.4	8.8	8.3	8.6
	314	9.6	10.6	8.8	9.9	7.0	8.5	9.0	7.8	7.3	7.4	8.7
	316	11.2	11.0	8.2	9.9	9.8	9.3	8.8	8.5	8.3	8.0	9.3
	317	13.3	8.3	9.6	10.6	8.9	10.5	9.2	9.5	10.1	10.9	12.1
	318	13.4	9.4	8.2	9.3	7.7	7.8	9.0	7.2	8.7	9.2	10.1
	321	11.7	11.2	7.3	11.1	8.7	7.3	6.9	7.4	9.3	9.6	12.0
	323	14.7	13.6	12.3	12.7	11.0	10.9	9.8	9.4	8.9	8.1	10.9
	324	15.5	13.7	11.6	10.1	11.1	10.1	11.2	10.6	10.1	10.1	10.2
	326	12.9	9.8	7.3	8.6	8.0	8.1	9.1	8.1	7.5	8.1	11.3
	328	14.4	14.0	10.6	11.4	10.1	10.0	9.5	9.6	9.5	10.4	9.8
	329	11.9	11.4	11.4	12.1	9.4	10.4	9.4	8.7	8.2	10.4	10.4
	331	10.1	8.5	7.9	8.5	7.9	7.7	9.1	6.5	7.6	7.5	7.5
	332	11.2	11.0	10.2	9.5	9.4	9.3	9.0	8.5	9.5	9.0	8.7
	333	14.7	11.0	11.8	12.2	12.1	10.7	9.6	9.5	10.3	10.3	10.1
335	9.3	9.7	8.6	8.7	7.1	8.2	7.8	7.0	5.9	6.1	7.7	
339	11.8	9.6	8.7	9.1	8.4	6.7	7.9	6.8	7.2	7.6	8.4	
340	13.8	10.8	9.9	7.6	6.7	7.4	7.6	7.3	7.6	9.0	9.1	
341	8.4	11.3	11.4	13.5	10.2	11.2	10.8	8.6	8.1	9.5	8.4	
	Ave.:	12.3	10.6	9.3	9.9	8.6	8.8	8.9	8.2	8.6	8.8	9.5

Bold indicates leukopenia (>40% reduction in WBC count compared to baseline count)

Nasal Swab Virus Shedding Results

Group	ID	Nasal Virus Titer (Log ₁₀ TCID ₅₀ /mL)													
		Vac ¹	Day Post-Challenge												
		-1	0	1	2	3	4	5	6	7	8	9	10		
Controls	308	0	0	0	0	0	0	0	0	1.7	0	0	0		
	315	0	0	0	0	0	0	1.9	0	1.9	1.7	0	1.9		
	319	0	0	0	0	0	0	0	0	1.7	2.1	1.7	0	0	
	320	0	0	0	0	0	0	0	0	0	1.7	0	0	0	
	322	0	0	0	0	0	0	0	0	0	0	1.7	0	0	
	325	0	0	0	0	0	0	0	0	1.7	2.1	1.7	1.7	2.1	
	327	0	0	0	0	0	0	0	0	0	0	1.7	0	0	
	330	0	0	0	0	0	0	0	0	0	1.9	1.9	2.1	1.9	
	334	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	336	0	0	0	0	0	0	0	0	1.9	2.3	2.3	1.7	0	0
	337	0	0	0	0	0	0	0	0	1.7	1.7	1.7	0	0	0
	338	0	0	0	0	0	0	0	0	0	3.1	1.7	1.7	1.9	0
		Ave.:	0	0	0	0	0	0	0	0.6	1.5	1.3	0.6	0.7	0
Vaccinates	309	0	0	0	0	0	0	0	0	0	0	0	0	0	
	310	0	0	0	0	0	0	0	0	0	0	0	0	0	
	311	0	0	0	0	0	0	0	0	0	0	0	0	0	
	312	0	0	0	0	0	0	0	0	0	0	0	0	0	
	313	0	0	0	0	0	0	0	0	0	0	0	0	0	
	314	0	0	0	0	0	0	0	0	0	0	0	0	0	
	316	0	0	0	0	0	0	0	0	0	0	0	0	0	
	317	0	0	0	0	0	0	0	0	0	0	0	0	0	
	318	0	0	0	0	0	0	0	0	0	0	0	0	0	
	321	0	0	0	0	0	0	0	0	0	0	0	0	0	
	323	0	0	0	0	0	0	0	0	0	0	0	0	0	
	324	0	0	0	0	0	0	0	0	0	0	0	0	0	
	326	0	0	0	0	0	0	0	0	0	0	0	0	0	
	328	0	0	0	0	0	0	0	0	0	0	0	0	0	
	329	0	0	0	0	0	0	0	0	0	0	0	0	0	
	331	0	0	0	0	0	0	0	0	0	0	0	0	0	
	332	0	0	0	0	0	0	0	0	0	0	0	0	0	
	333	0	0	0	0	0	0	0	0	0	0	0	0	0	
	335	0	0	0	0	0	0	0	0	0	0	0	0	0	
	339	0	0	0	0	0	0	0	0	0	0	0	0	0	
340	0	0	0	0	0	0	0	0	0	0	0	0	0		
341	0	0	0	0	0	0	0	0	0	0	0	0	0		
	Ave.:	0	0	0	0	0	0	0	0	0	0	0	0	0	

¹ Prior to vaccination, Study day 0

Clinical Observations Post-Challenge

Group	ID	Day Post-Challenge														Affected*		
		-1	0	1	2	3	4	5	6	7	8	9	10	11	12		13	14
Controls	308	0	0	0	0	0	0	0	C1	0	N2	0	D2	D2,N1	0	0	0	Yes
	315	0	C1	0	0	0	0	C1	C1	C2	C2	C2	N2,C1	N2,C2	0	0	C2	Yes
	319	0	0	0	0	0	0	0	0	N2	N2	0	N1,C1	N1	N1	0	0	Yes
	320	0	0	0	0	0	0	0	0	0	0	0	N1	0	0	0	0	No
	322	0	0	0	0	0	0	0	0	0	0	N1	0	0	0	0	0	No
	325	0	0	0	0	0	0	0	0	0	0	0	N1	N1	N1	0	C1	No
	327	0	0	0	0	0	N1	N1	N1	0	N2	0	N1	N1	N2	0	0	Yes
	330	0	0	0	0	0	0	0	0	0	0	0	0	D2,N1	D1	0	0	Yes
	334	0	0	0	0	0	0	C1	0	0	C2	0	0	0	N1	0	0	No
	336	0	0	0	0	0	0	0	0	0	N1,C1	0	0	0	0	0	0	No
	337	0	0	0	0	0	0	0	0	0	0	0	C1	0	0	0	0	No
	338	0	0	0	0	0	0	0	0	0	0	0	N1	D2,N1	0	0	0	Yes
	Vaccinates	309	0	0	0	0	0	0	0	0	0	0	0	D1	0	0	0	No
310		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
311		0	0	0	0	0	0	0	0	0	0	0	0	D1	0	0	0	No
312		0	0	0	0	0	0	0	0	0	0	0	0	C1	0	0	0	No
313		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
314		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
316		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
317		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
318		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
321		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
323		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
324		0	0	0	0	0	N1	0	0	0	N1	N1	0	C1	0	0	0	No
326		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
328		0	0	0	0	0	0	0	0	0	0	0	0	D1	C1	0	0	No
329		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
331		0	0	0	0	0	0	0	N1	N1	D1,N1	D2	0	0	0	0	0	Yes
332		0	0	0	0	0	0	0	0	0	0	0	D1	0	0	0	0	No
333		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
335		0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No
339		0	0	0	0	0	0	0	0	0	0	0	0	D1	0	0	0	No
340	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No	
341	0	0	0	0	0	0	0	C1	0	0	0	0	0	0	0	0	No	

Clinical Description: 0 = Normal, C = Cough, D = Diarrhea, N = Nasal Discharge

*An affected calf is one with a moderate to severe clinical sign of diarrhea, nasal discharge or depression on any post-challenge day

Clinical Score	Diarrhea	Nasal Discharge	Depression	Dyspnea	Cough
0	None	None	None	None	None
1	Soft feces	Serous discharge	Moves slowly, head down	Short and rapid	< 3 episodes
2	Watery diarrhea	Mucopurulent discharge	Tends to lie down, staggers	Labored, noticeable abdominal	> 3 episodes
3	Watery and bloody diarrhea	Severe mucopurulent discharge	Stands with difficulty	Very labored, grunting	NA

Study Type	Efficacy
Pertaining to	Bovine Viral Diarrhea Virus Type 2 (BVDV2)
Study Purpose	To demonstrate efficacy against respiratory disease caused by BVDV2.
Product Administration	
Study Animals	Bovine
Challenge Description	BVDV2a strain 1373
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	December 10, 2003

Study Type	Efficacy
Pertaining to	Bovine Viral Diarrhea Virus Type 1 (BVDV2)
Study Purpose	To demonstrate efficacy against persistent infection of calves caused by BVDV2
Product Administration	
Study Animals	Bovine
Challenge Description	BVDV Type 2 strain SD02 BVD05
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	April 25, 2005

Study Type	Efficacy																																																
Pertaining to	Bovine Viral Diarrhea Virus Type 2 (BVDV2)																																																
Study Purpose	To demonstrate efficacy against respiratory disease caused by BVDV2 1 year after vaccination.																																																
Product Administration	1 dose administered by the subcutaneous route																																																
Study Animals	40 calves, 3 months of age; 20 vaccinates, 20 controls																																																
Challenge Description	All calves were challenged with BVDV2a strain 1373 384 days after vaccination.																																																
Interval observed after challenge	All calves were monitored daily for 14 days post-challenge for clinical signs of disease.																																																
Results	<p><u>Mortality:</u> An affected calf was one that died or was humanely euthanized due to severe BVDV2 disease during the post-challenge period.</p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># Affected</th> <th>Percent (%)</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>20</td> <td>0</td> <td>0</td> </tr> <tr> <td>Controls</td> <td>20</td> <td>11*</td> <td>55</td> </tr> </tbody> </table> <p>* An additional 7 control calves either died or were euthanized by day 16 post-challenge (2 days after the post-challenge observation period) due to severe BVDV2 clinical disease, bringing the mortality rate to 90% for control calves.</p> <p><u>Leukopenia:</u> An affected calf was one that showed a post-challenge WBC count $\leq 60\%$ of the baseline WBC count, and/or $\leq 4.0 \times 10^3$ WBC/μL.</p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># Affected</th> <th>Percent (%)</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>20</td> <td>3</td> <td>15</td> </tr> <tr> <td>Controls</td> <td>20</td> <td>19</td> <td>95</td> </tr> </tbody> </table> <p><u>Virus Shedding:</u> An affected calf was one in which nasal virus shedding was detected on any day post-challenge.</p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># Affected</th> <th>Percent (%)</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>20</td> <td>0</td> <td>0</td> </tr> <tr> <td>Controls</td> <td>20</td> <td>20</td> <td>100</td> </tr> </tbody> </table> <p><u>Clinical Observations:</u> An affected calf showed moderate to severe signs of acute BVD2 (i.e. moderate to severe diarrhea, nasal discharge, depression, dyspnea, oral lesions, or mortality) on any day during the observation period.</p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># Affected*</th> <th>Percent (%)</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>20</td> <td>2</td> <td>10</td> </tr> <tr> <td>Controls</td> <td>20</td> <td>20</td> <td>100</td> </tr> </tbody> </table> <p>Raw data shown on attached pages.</p>	Group	# of Animals	# Affected	Percent (%)	Vaccinates	20	0	0	Controls	20	11*	55	Group	# of Animals	# Affected	Percent (%)	Vaccinates	20	3	15	Controls	20	19	95	Group	# of Animals	# Affected	Percent (%)	Vaccinates	20	0	0	Controls	20	20	100	Group	# of Animals	# Affected*	Percent (%)	Vaccinates	20	2	10	Controls	20	20	100
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USDA Approval Date	September 19, 2014																																																

White Blood Cell (WBC) Counts (x 10³/μL)

Group	ID	Day Post-Challenge														
		-2	-1	0	Baseline	2	3	4	5	6	7	8	9	10	12	14
Controls	195	11.1	11.0	11.1	11.1	11.4	6.7	6.6	6.1	6.3	7.1	6.7	4.9	4.3	4.4	3.9
	198	10.6	11.2	10.7	10.8	9.4	5.8	5.2	4.9	5.0	4.8	4.0	6.4	7.0	Dead	Dead
	199	8.4	8.4	9.8	8.9	8.6	5.2	5.3	5.5	5.8	4.9	3.9	4.0	2.7	3.1	Dead
	202	7.0	6.5	7.0	6.8	7.4	3.7	4.4	4.1	4.3	4.3	3.4	4.8	6.5	4.3	7.2
	204	11.1	8.8	16.7	12.2	14.7	8.0	8.5	8.8	8.4	10.0	7.4	5.8	4.0	4.4	Dead
	206	9.1	8.9	8.5	8.8	8.5	4.4	4.9	4.7	4.5	4.9	3.5	2.5	2.7	2.2	Dead
	207	9.9	10.5	9.9	10.1	9.8	5.3	6.7	7.5	6.6	6.2	5.5	3.9	3.6	5.2	Dead
	209	11.9	11.5	10.7	11.4	11.6	6.6	8.5	6.8	7.4	7.1	5.1	4.0	4.6	Dead	Dead
	211	8.1	8.5	8.1	8.2	7.8	4.9	6.6	5.5	5.1	4.9	3.8	3.2	2.4	1.9	Dead
	212	11.4	13.5	9.9	11.6	7.7	5.7	5.0	6.1	6.1	6.0	5.3	3.9	3.0	3.7	3.0
	213	10.5	8.6	8.4	9.2	9.8	6.5	6.8	6.3	6.3	5.0	5.3	2.8	2.1	2.2	1.4
	218	10.9	10.3	10.3	10.5	9.6	5.6	6.5	6.4	6.1	5.8	8.3	11.3	10.7	7.5	8.8
	219	14.5	15.0	14.1	14.5	14.5	10.7	11.5	10.2	10.8	8.4	8.9	5.6	5.0	6.6	Dead
	220	9.2	8.8	8.4	8.8	8.3	7.1	6.5	5.5	5.6	5.2	5.6	4.9	3.6	3.9	3.0
	221	9.3	10.0	10.3	9.9	8.1	6.5	6.0	6.9	6.1	4.7	3.2	2.8	2.6	1.6	Dead
	222	11.1	8.3	8.7	9.4	10.0	5.6	6.1	6.2	7.1	6.0	5.7	5.6	11.1	Dead	Dead
	223	16.2	14.7	15.9	15.6	13.6	12.0	12.3	11.4	11.2	9.7	9.4	6.8	5.3	4.2	Dead
	227	12.1	10.6	10.6	11.1	12.0	8.7	7.9	8.7	8.4	7.8	7.6	9.6	10.1	10.6	9.2
	230	11.6	11.2	11.3	11.4	11.9	9.3	8.6	8.5	8.4	8.4	6.2	6.4	7.5	8.2	13.0
	231	7.3	7.1	7.3	7.2	7.6	6.9	6.0	6.5	5.2	5.1	3.8	3.9	3.4	3.0	1.8
	Ave.:				10.4	10.1	6.8	7.0	6.8	6.7	6.3	5.6	5.2	5.1	4.5	5.7
Vaccinates	194	18.4	17.3	18.7	18.1	18.9	16.7	13.9	15.1	16.7	18.7	16.2	16.4	17.2	16.4	17.1
	196	8.1	7.5	8.4	8.0	9.4	10.5	7.6	5.9	7.3	6.9	7.7	7.6	8.3	8.8	8.1
	197	14.6	13.7	14.0	14.1	13.5	13.8	13.2	12.5	11.3	12.5	11.6	13.1	13.1	13.3	13.4
	200	8.1	8.7	10.4	9.1	12.5	9.3	9.0	8.4	8.0	7.7	9.6	8.5	7.9	7.4	7.2
	201	10.8	9.8	8.5	9.7	8.2	7.3	5.2	6.5	5.8	7.9	8.4	8.3	7.8	7.1	7.4
	203	9.8	10.7	10.5	10.3	8.4	5.1	5.4	5.6	6.7	6.6	10.6	10.7	8.0	8.8	6.6
	205	9.3	10.7	10.9	10.3	9.3	8.0	6.8	5.5	6.4	9.6	10.5	10.6	9.8	9.5	9.9
	208	8.6	9.9	8.5	9.0	8.3	9.0	9.7	7.1	7.7	7.0	8.9	9.2	9.8	6.9	7.6
	210	11.1	11.0	11.1	11.1	11.9	9.7	8.9	9.1	10.4	10.0	11.1	9.5	9.1	9.7	9.0
	214	15.5	18.2	15.7	16.5	22.6	16.4	15.1	13.1	13.0	15.4	15.8	15.4	18.6	14.1	14.2
	215	8.4	9.5	8.8	8.9	8.3	8.0	6.9	6.5	6.6	8.4	8.7	9.1	8.9	8.9	8.9
	216	10.1	10.5	11.0	10.5	12.1	9.8	7.0	6.7	6.8	8.2	10.3	9.1	9.1	8.2	8.6
	217	12.1	13.6	13.2	13.0	13.4	13.7	12.5	11.2	12.4	14.7	14.1	12.8	10.2	10.9	12.3
	224	10.4	9.0	8.6	9.3	10.7	9.5	7.7	7.5	7.2	9.3	7.7	8.1	10.5	8.8	10.5
	225	10.7	11.5	10.5	10.9	10.3	11.3	10.5	8.0	7.8	7.5	10.8	10.6	12.5	10.7	10.4
	226	9.2	8.3	9.7	9.1	10.4	9.9	9.1	9.1	8.4	8.4	8.7	9.3	10.2	8.7	9.0
	228	8.3	8.0	7.4	7.9	8.4	7.7	6.4	5.4	6.4	7.1	9.4	7.9	8.6	7.2	7.1
229	7.4	7.6	7.0	7.3	7.2	7.3	7.0	7.3	6.8	6.6	6.9	6.3	5.5	7.1	7.5	
232	11.1	10.7	11.3	11.0	10.7	10.0	8.7	8.5	8.2	12.0	10.3	9.3	9.4	7.6	8.0	
233	15.3	16.2	14.0	15.2	14.1	13.8	11.6	11.6	11.2	13.9	13.4	14.2	14.1	14.8	12.9	
	Ave.:				11.0	11.4	10.3	9.1	8.5	8.8	9.9	10.5	10.3	10.4	9.7	9.8

Bold indicates leukopenia (WBC count ≤ 60% of baseline count, and/or WBC count ≤ 4.0 x 10³/μL)

Nasal Swab Virus Shedding Results

Group	ID	Nasal Virus Titer (Log ₁₀ FAID ₅₀ /mL) Day Post-Challenge														
		Vac. ¹	-1	0	1	2	3	4	5	6	7	8	9	10	12	14
Controls	195	0	0	0	0	0	0	0	0	0	0	1.7	2.3	2.5	1.7	C ²
	198	0	0	0	0	0	0	0	0	1.7	2.5	2.5	2.5	1.7	Dead	Dead
	199	0	0	0	0	0	0	0	0	0	0	1.9	2.5	2.5	0	Dead
	202	0	0	0	0	0	0	1.7	0	1.9	2.3	1.7	2.3	2.1	0	0
	204	0	0	0	0	0	0	0	0	0	0	1.9	2.9	3.9	2.5	Dead
	206	0	0	0	0	0	0	0	0	0	2.1	0	2.1	3.1	0	Dead
	207	0	0	0	0	0	0	0	0	1.9	0	2.5	2.7	2.9	2.7	Dead
	209	0	0	0	0	0	0	0	0	0	1.7	2.3	2.5	2.9	Dead	Dead
	211	0	0	0	0	0	0	0	1.7	1.9	0	2.1	3.5	3.5	3.9	Dead
	212	0	0	0	0	0	0	0	0	0	0	1.7	2.7	2.3	0	0
	213	0	0	0	0	0	0	0	0	0	1.9	2.3	3.5	3.5	3.3	2.1
	218	0	0	0	0	0	0	0	0	0	0	0	1.7	0	0	0
	219	0	0	0	0	0	0	0	0	0	1.9	2.1	0	2.7	1.7	Dead
	220	0	0	0	0	0	0	0	0	0	0	2.3	2.7	3.5	3.5	3.9
	221	0	0	0	0	0	0	0	1.7	0	2.3	2.1	3.9	3.5	4.1	Dead
	222	0	0	0	0	0	0	0	0	0	1.9	2.5	2.9	2.5	Dead	Dead
	223	0	0	0	0	0	0	0	0	0	0	1.9	2.3	2.5	0	Dead
	227	0	0	0	0	0	0	0	0	0	0	0	0	1.9	0	0
230	0	0	0	0	0	0	0	0	0	1.9	1.7	3.1	1.9	0	0	
231	0	0	0	0	0	0	0	0	0	0	0	3.1	2.3	1.9	1.7	
	Ave.:	0	0	0	0	0	0	0.1	0.2	0.4	0.9	1.7	2.5	2.6	1.5	1.0
Vaccinates	194	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	196	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	197	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	200	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	201	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	203	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	205	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	208	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	210	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	214	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	215	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	216	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	217	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	224	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	225	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	226	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	228	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	229	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
232	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
233	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	
	Ave.:	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

¹Prior to vaccination, Study day 0

²Contaminated sample

Clinical Observation Post-Challenge

Group	ID	Day Post-Challenge														Affected	Died/Euthanized			
		-1	0	1	2	3	4	5	6	7	8	9	10	11	12			13	14	
Controls	195	0	0	0	0	0	0	0	0	N1	N1	N1	N1,OL1	N2,D2,A1,OL3	NA	NA	D3,A2,R2,OL3	Yes	No ¹	
	198	0	0	0	0	0	0	0	0	N1,C1	N1	N1	N1,OL1	Died	NA	NA	NA	Yes	Yes	
	199	0	0	0	0	0	0	0	0	N1	N1	N1	N3,OL1	N3,D2,A3,R2,OL3,Euth.	NA	NA	NA	Yes	Yes	
	202	0	0	0	0	0	0	0	0	N1	N1	N2,D1	N3,A1,OL1	N3,D2,OL2	N1,A1	N2,A1,OL2	NA	Yes	No ¹	
	204	N1	0	0	0	0	0	0	0	N1	N1	N1,D1	N2,OL2	N1,D1,A1,OL2	Died	NA	NA	Yes	Yes	
	206	0	0	0	0	0	0	0	0	N1	N1	0	N3,OL2	N3,D1,A2,R2,OL2	Died	NA	NA	Yes	Yes	
	207	N1	0	0	0	0	0	0	0	N1	N1,D1	N1	N1	N1,D2,A1	N3,D3,R2,A3,Euth.	NA	NA	Yes	Yes	
	209	0	0	0	0	0	0	0	0	N1	N1	N1	N1,D2	N1,D2,A1,R2,OL1	Died	NA	NA	Yes	Yes	
	211	0	0	0	0	0	0	0	0	N1	N1,D1	N1	N1	N1,D2,A1	N3,A1,OL2	N2,D2,A2,OL3,Euth.	NA	Yes	Yes	
	212	N1	0	0	0	0	0	0	0	N1	N1	N1	N3,D1	N1	N1	N2,D1,A1	N1,A1,OL1	Yes	No ¹	
	213	N1	0	0	0	0	0	0	0	N1	N1	N1	N2,OL2	N1,OL2	A1,OL3,Bleeding	N1,A2,R2,OL3	NA	Yes	No ¹	
	218	N1	N1	0	0	0	0	0	0	N1	N1	N2	N2	N1	N1	N1	N1	NA	Yes	No
	219	0	0	0	0	0	0	0	0	N1	N1	N1	N3,OL2	N2,A1,OL2	N2,D2,A3,R2,OL2,Euth.	NA	NA	Yes	Yes	
	220	N1	0	0	0	0	0	0	0	N1	N1	N1	N1	N1	N2,A1	N3,A1	N2,A1,OL2	Yes	No ¹	
	221	0	0	0	0	0	0	0	0	N1	N2	N1	N1	N2,D1,A1,OL3	N2,OL3	Died	NA	Yes	Yes	
	222	N1	0	0	0	0	0	0	0	N1	N1	N2	N1,OL1	N1	Died	NA	NA	Yes	Yes	
	223	N1	0	0	0	0	0	0	0	N1	N1	N1	N1	N1,A2,R2	N1,A3,R3,Euthanized	NA	NA	Yes	Yes	
	227	0	0	0	0	0	0	0	0	N1	N1	N1	N1	N2,D2,A1,OL1	N1,D2,A1	0	N1,A1	Yes	No ¹	
	230	0	0	0	0	0	0	0	0	N1	N2	N2	N2	N2,A1,R1,OL1	N1,OL1	N2,A2,OL1,Bleeding	A2,OL2	Yes	No ¹	
	231	0	N1	0	0	0	0	0	0	N1	N1	N1	N1	N1,D1	N2,OL3	N3,D2,A1	N1,D2,A1	Yes	No ¹	
	Vaccinates	194	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	No	No
		196	0	N1	0	0	0	0	0	0	N1	0	N1	N1	N1	N1	N1	N1	No	No
		197	0	0	0	0	0	0	0	0	N1	0	N1	N1	N1	N1	N1	0	No	No
200		0	0	0	0	0	0	0	0	0	0	N1	0	N1	N1	N1	0	No	No	
201		N1	0	0	0	0	0	0	0	N1	0	0	N1	N1	N1	0	0	0	No	No
203		0	0	0	0	0	0	0	0	N1	N1,D1	D1	N1,D1	N1,D1	0	0	0	No	No	
205		N1	N1	0	0	0	0	0	0	N1	N1	N1	N1	0	N2	N1	N1	Yes	No	
208		0	0	0	0	0	0	0	0	N1	0	N1	N1	N1	N1	N1	0	No	No	
210		0	N1	0	0	0	0	0	0	N1	0	0	N1	N1	N1	N1	0	No	No	
214		0	N1	0	0	0	0	0	0	N1	0	N1	N1	N1	N1	N1	0	No	No	
215		0	N1	0	0	0	0	0	0	N1	N1	N1	N1,D1	N1	N1,D1	N1,D1	N1	No	No	
216		0	0	0	0	0	0	0	0	N1	N1	N1	N1	N1,D1	0	N1	0	No	No	
217		0	0	0	0	0	0	0	0	N1	D1	N1,D1	N1	N1	N1	N1	0	No	No	
224	0	0	0	0	0	0	0	0	N1	0	N1	N1	N1,D1	0	N1,D1	N1	No	No		
225	0	0	0	0	0	0	0	0	0	0	0	N1	N1	N1	N1	0	No	No		
226	0	0	0	0	0	0	0	0	0	0	0	N1	N1,D1	0	N1	0	No	No		
228	N1	0	0	0	0	0	0	0	N1	0	0	N1	N1	N1	0	0	0	No	No	
229	0	0	0	0	0	0	0	0	N1,D1	0	0	N2	N1	N1	N2	N1	Yes	No		
232	0	N1	0	0	0	0	0	0	N1	0	0	N1	N1	N1	0	0	0	No	No	
233	N1	0	0	0	0	0	0	0	N1	0	N1	N1	N1	0	N1	0	0	No	No	

Clinical Descriptions: 0 = Normal, N = Nasal Discharge, D = Diarrhea, A = Depression, R = Dyspnea, OL = Oral Lesion, NA = Not observed, Severity: 1 = mild, 2 = moderate, 3 = severe
¹Animal died or was euthanized by 16 days post-challenge (20-Dec-13)

Clinical Score	Diarrhea	Nasal Discharge	Depression (Attitude)	Dyspnea	Oral Lesions
0	None	None	Normal	None	None
1	Soft feces	Serous discharge	Moves slowly, head down	Short and rapid	Erosions on oral mucosa
2	Watery diarrhea	Mucopurulent discharge	Tends to lie down, staggers	Labored, abdominal breathing	Ulcerations on oral mucosa
3	Watery and bloody diarrhea	Severe mucopurulent	Stands with difficulty	Very labored, grunts or raspy breathing	Hemorrhages on oral mucosa

Study Type	Efficacy																								
Pertaining to	Bovine Viral Diarrhea Virus Type 2 (BVDV2)																								
Study Purpose	To demonstrate efficacy against fetal infection caused by BVDV2 206 days after vaccination.																								
Product Administration	1 dose administered by the subcutaneous route 28 days prior to breeding.																								
Study Animals	46 seronegative heifers, 28 vaccinates and 18 controls.																								
Challenge Description	All heifers were challenge with BVDV2 strain IV809-04 at 164-178 days of gestation.																								
Interval observed after challenge	Blood samples were collected on days 0, 5 through 10 post challenge for virus isolation. Fetuses were collected on day 60 after challenge.																								
Results	<p><u>Virus Isolation on heifers:</u></p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># Affected</th> <th>Percent (%)</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>28</td> <td>2</td> <td>7</td> </tr> <tr> <td>Controls</td> <td>18</td> <td>18</td> <td>100</td> </tr> </tbody> </table> <p><u>Virus Isolation from fetal samples:</u> Calves (fetuses) were considered positive if virus was isolated from any fetal tissue (lung, spleen, thymus, kidney, buffy coat).</p> <table border="1"> <thead> <tr> <th>Group</th> <th># of Animals</th> <th># Affected</th> <th>Percent (%)</th> </tr> </thead> <tbody> <tr> <td>Vaccinates</td> <td>28</td> <td>2</td> <td>4</td> </tr> <tr> <td>Controls</td> <td>18</td> <td>17</td> <td>94</td> </tr> </tbody> </table> <p>Raw data shown on attached pages.</p>	Group	# of Animals	# Affected	Percent (%)	Vaccinates	28	2	7	Controls	18	18	100	Group	# of Animals	# Affected	Percent (%)	Vaccinates	28	2	4	Controls	18	17	94
Group	# of Animals	# Affected	Percent (%)																						
Vaccinates	28	2	7																						
Controls	18	18	100																						
Group	# of Animals	# Affected	Percent (%)																						
Vaccinates	28	2	4																						
Controls	18	17	94																						
USDA Approval Date	October 4, 2007																								

Viremia of Challenged Heifers

(Vaccinate Group)

Heifer Number	Isolation of BVDV from Buffy-coats at Days post-challenge						
	0	5	6	7	8	9	10
1536	0	0	0	0	0	0	0
1538	0	0	0	0	0	0	0
1541	0	0	0	0	0	0	0
1544	0	0	1	0	0	0	0
1545	0	0	0	0	0	0	0
1556	0	0	0	0	0	0	0
1558	0	0	0	0	0	0	0
1562	0	0	0	0	0	0	0
1566	0	0	0	0	0	0	0
1567	0	0	0	0	0	0	0
1569	0	0	0	0	0	0	0
1570	0	0	0	0	0	0	0
1575	0	0	0	0	0	0	0
1581	0	0	0	0	0	0	0
1582	0	0	0	0	0	0	0
1585	0	0	1	0	0	0	0
1594	0	0	0	0	0	0	0
1596	0	0	0	0	0	0	0
1597	0	0	0	0	0	0	0
1598	0	0	0	0	0	0	0
1599	0	0	0	0	0	0	0
1601	0	0	0	0	0	0	0
1605	0	0	0	0	0	0	0
1606	0	0	0	0	0	0	0
1607	0	0	0	0	0	0	0
1608	0	0	0	0	0	0	0
1609	0	0	0	0	0	0	0
1614	0	0	0	0	0	0	0

0=negative; 1=positive.

(Control Group)

Heifer Number	Isolation of BVDV from Buffy-coats at Days post-challenge						
	0	5	6	7	8	9	10
1540	0	1	1	1	1	0	0
1542	0	1	1	0	1	0	0
1543	0	1	1	1	1	0	1
1546	0	0	1	1	1	0	0
1549	0	1	1	1	1	1	0
1553	0	1	1	1	1	1	0
1557	0	0	1	1	1	0	0
1571	0	1	1	1	1	0	0
1572	0	1	1	0	1	0	0
1573	0	1	1	1	1	0	0
1574	0	1	1	1	0	1	0
1577	0	1	1	1	0	0	0
1586	0	1	1	1	0	0	0
1590	0	1	1	1	0	0	0
1591	0	1	1	1	1	1	0
1593	0	1	1	1	1	1	0
1595	0	1	1	1	1	1	0
1615	0	1	0	0	0	1	0

0=negative; 1=positive.

Virus Isolation from Fetal Samples

Groups	Heifer ID	Virus isolations					VI Results
		Thymus	Spleen	Lung	Kidney	Buffy-coats	
Vaccinate	1536	0	0	0	0	0	0
	1538	0	0	0	0	0	0
	1541	0	0	0	0	0	0
	1544	0	0	0	0	0	0
	1545	1	1	1	0	1	1
	1556	0	0	0	0	0	0
	1558	0	0	0	0	0	0
	1562	0	0	0	0	0	0
	1566	0	0	0	0	0	0
	1567	0	0	0	0	0	0
	1569	0	0	0	0	0	0
	1570	0	0	0	0	0	0
	1575	0	0	0	0	0	0
	1581	0	0	0	0	0	0
	1582	0	0	0	0	0	0
	1585	0	0	0	0	0	0
	1594	0	0	0	0	0	0
	1596	0	0	0	0	0	0
	1597	0	0	0	0	0	0
	1598	0	0	0	0	0	0
	1599	0	0	0	0	0	0
1601	0	0	0	0	1	1	
1605	0	0	0	0	0	0	
1606	0	0	0	0	0	0	
1607	0	0	0	0	0	0	
1608	0	0	0	0	0	0	
1609	0	0	0	0	0	0	
1614	0	0	0	0	0	0	

Groups	Heifer ID	Virus isolations					VI Results
		Thymus	Spleen	Lung	Kidney	Buffy-coats	
Controls	1540	1	1	1	1	1	1
	1542	1	1	1	1	0	1
	1543	0	0	0	0	1	1
	1546	0	0	0	0	1	1
	1549	1	1	1	1	1	1
	1553	1	1	1	1	1	1
	1557	1	1	1	1	1	1
	1571	0	0	0	0	0	0
	1572	0	0	0	0	1	1
	1573	0	0	0	0	1	1
	1574	1	1	1	1	0	1
	1577	0	0	0	0	1	1
	1586	1	1	1	1	0	1
	1590	1	1	1	1	0	1
	1591	1	1	1	1	0	1
	1593	0	1	0	1	1	1
	1595	1	1	1	1	1	1
1615	0	0	0	0	1	1	

Study Type	Safety
Pertaining to	ALL
Study Purpose	To demonstrate safety under field conditions.
Product Administration	
Study Animals	Bovine
Challenge Description	
Interval observed after challenge	
Results	Study data were evaluated by USDA-APHIS prior to product licensure and met regulatory standards for acceptance at the time of submission. No data are published because this study was submitted to USDA-APHIS prior to January 1, 2007, and APHIS only requires publication of data submitted after that date.
USDA Approval Date	June 16, 2004

Study Type	Safety
Pertaining to	ALL
Study Purpose	To demonstrate safety in pregnant animals under field conditions when cows or heifers are vaccinated prior to breeding, within the previous 12 months, with a modified live Infectious Bovine Rhinotracheitis Virus (IBRV) and Bovine Viral Diarrhea Virus (BVDV) product
Product Administration	Two doses, administered subcutaneously. First vaccination given 14 to 60 days prior to breeding. Second vaccination given during a specified trimester of pregnancy.
Study Animals	1 st Trimester Study: 468 pregnant heifers (52 – 86 days pregnant) 2 years of age and older. 2 nd Trimester Study: 461 pregnant heifers (100 – 180 days pregnant) 2 – 14 years of age. 3 rd Trimester Study: 440 pregnant heifers (≥190 days pregnant) 2 years of age and older.
Challenge Description	Not applicable
Interval observed after challenge	All cows were observed from pre-breeding vaccination through calving.
Results	Summary of the results listed in the table below
USDA Approval Date	May 9, 2013

Summary of the results as follows:

Trimester	Group	No. of Cows		Fetal Loss (%) related to vaccination	Fetal Loss (%) unrelated to vaccination as affirmed by licensee
		Entered	Removed*		
1 st	Vaccinates	235	4	1 (0.4 %)	3 (1.3%)
	Controls	233	7	2 (0.9%)	2 (0.9%)
2 nd	Vaccinates	231	2	1 (0.4%)	6 (2.5%)
	Controls	230	0	1 (0.4%)	2 (0.8%)
3 rd	Vaccinates	216	1	0 (0%)	8 (3.7%)
	Controls	224	2	1 (0.5%)	5 (2.2%)

*Number of cows removed from the study results due to death serious illness considered unrelated to vaccination as affirmed by licensee